REMARKS/ARGUMENTS

The Cross-References to Related Applications section of the specification has been amended to delete the priority claims to US Application Nos. 09/322,289, 09/201,430 and 60/080,970. A supplemental Application Data Sheet which deletes the priority claims to US Application Nos. 09/322,289, 09/201,430, and 60/080,970 is submitted herewith

The term "pharmaceutical" has been deleted from the claims. The previous reference to a CRM197 carrier has been broadened to refer to a toxoid from a pathogenic bacterium, as described at e.g., paragraph [0126]. CRM197 continues to be specified in dependent claims. The specification has been amended to include a specific reference to CRM197 among the list of recited carriers. Support is provided in application US Application No. 09/201,430 in the paragraph bridging pp. 4-5, which is incorporated by reference into the present application. The claims have also been amended more clearly to state that the Aβ peptide is Aβ1-7 in view of the Examiner's position that the claims read on longer Aβ peptides, such as Aβ1-9. The claims use the transitional term "comprising" because they can include elements other than Aβ (e.g., a carrier, a linker, and/or an excipient). However, the use of this transitional term does not leave the claim open to elements that would be inconsistent with the express recitals, in this case, the express recital of the presence of an Aβ peptide that is Aβ1-7.

This response is accompanied by a change of inventorship that changes the inventorship to Dale Schenk alone. The application was originally filed with a different set of claims than is now being pursued, and the inventorship is being amended to conform to the claims now pending.

No amendment should be construed as acquiescence in any ground of rejection, nor should the provision of the 131 declaration discussed below. Lack of comment on any of the Examiner's remarks should not be viewed as acquiescence therein.

Rejections Under 35 U.S.C. § 103(a)

Claims 119, 121-124, 126-131 and 134-137 and 139-143 continued to stand rejected as allegedly obvious over Chain (December 1999) as evidenced by Alberts (1989) in

view of Frenkel (February 1999), Collier (1997) and Van den Dobbelsteen (1995). Chain is alleged to teach immunizing with a chimeric peptide including a T-helper epitope and a peptide from the N or C terminus of Aβ. Chain is also alleged to teach adjuvants. The Examiner acknowledges Chain does not teach either Aβ1-7 or CRM197. Frenkel is alleged to teach that residues Aβ1-7 encompass an important site of Aβ for the generation of antibodies capable of inhibiting Aβ aggregation. Collier and Van den Dobbelsteen are cited as teaching use of diphtheria toxin in vaccines including CRM 197.

The applicant maintains the distinctions over the references discussed in the previous response but will not repeat them here. Instead, the applicant provides a declaration under 37 C.F.R. § 1.131 by inventor Dale Schenk. The declaration provides evidence that Dr. Schenk had reduced to practice a composition comprising Aβ1-5 linked to an immunoglobulin carrier and an adjuvant before December 8, 1999 (the priority date alleged for Chain). The experiment reducing Aβ1-5 to practice is contained within the present application as Example IV (Schenk at ¶5). As discussed by Dr. Schenk, the experiment is also described in his predecessor application US Application No. 09/201,430 filed in 1998. Thus, there is no doubt that the experiment was performed before the alleged priority date of Chain. Dr. Schenk concluded from the data that Aβ1-5 linked to an immunoglobulin carrier reduced levels of Aβ in the brain of a transgenic mouse model of Alzheimer's disease (Schenk at ¶6).

The declaration also provides evidence that Dr. Schenk had conceived a composition comprising Aβ1-7 linked to a tetanus toxoid carrier and an adjuvant before December 8, 1999, and had diligently reduced it to practice thereafter (Schenk at ¶7). This experiment is described in Example XVI of the present application. That conception had occurred before December 8, 1999 is shown by a memo between two of Dr. Schenk's colleagues requesting synthesis of such a peptide by an outside supplier (Schenk at ¶8). The peptide was first injected into a mouse model with complete Freund's adjuvant on September 23, 1999 (Schenk at ¶10). Further, injections were performed at intervals of about 2 or 4 weeks until the last injection was performed March 9, 2000 (Schenk at ¶11). Thereafter, the mice were sacrificed, brain tissue from the mice was extracted and homogenized, and Aβ levels were

measured by ELISA (Schenk at ¶12). The data from this experiment (and similar experiments on other immunogens performed contemporaneously) were written up in a Quarterly Report dated April 20, 2000 (Schenk ¶12). Dr. Schenk concluded from the data in the quarterly report that the Aβ1-7 conjugate was effective in reducing levels of Aβ in the brain of a mouse model of Alzheimer's disease (Schenk at ¶13). It is respectfully submitted that this chronology demonstrates conception before December 8, 1999, reduction to practice by at least April 20, 2000, and diligence between these dates.

An applicant may overcome a 35 U.S.C. § 103 rejection based on a combination of references by showing completion of the whole invention or something falling within the claims prior to the date of any one of the references. MPEP § 715.02. An applicant can also antedate a combination of references A and B, when B was published earlier than A, by showing possession of A alone. *Id.* Insofar as the present claims are alleged to have been obvious over Chain, it is respectfully submitted that the present inventor's actual reduction to practice of Aβ1-5 linked to an immunoglobulin carrier and an adjuvant before December 8, 1999 shows the inventor's possession of at least the subject matter of Chain that is alleged to render the claimed invention obvious. Because the other references with which Chain is being combined are published before Chain's alleged priority date, showing possession of the subject matter disclosed by Chain is sufficient to antedate the combination of references. Furthermore, the present inventor's conception of Aβ1-7 linked to a toxoid carrier and an adjuvant before December 8, 1999 and diligent reduction to practice thereafter shows possession of at least a species of the claimed invention before the priority date of Chain. Such a showing is by itself sufficient to remove Chain as prior art. For either of these reasons, it is respectfully submitted that Chain is not prior art, and the rejection should be withdrawn.

Claims 120 and 132 stand rejected over the previous combination of references in further view of Potter (1998) and Restifo (1998). Potter and Restifo are cited as teaching that the immunogenicity of small peptides can be increased by using multiple copies of the peptides. Insofar as claims 120 and 132 are alleged to have been obvious over Chain and other references

published before Chain, Chain is not prior art for at least the same reasons as discussed in connection with claims 119.

Claims 125 and 138 stand rejected over Chain as evidenced by Alberts in view of Frenkel, Collier and Van den Dobbelsteen in further view of Peeters (1989). Peeters is alleged to teach the effect of four chemical crosslinkers on immunogenicity of peptide-carrier conjugates. Insofar as claims 125 and 138 are alleged to have been obvious over Chain in combination with other references published before Chain, Chain is not prior art for the same reasons as discussed in connection with claim 119.

Claim 133 is rejected as allegedly obvious over Chain as evidenced by Alberts in view of Frenkel, Collier and Van den Dobbelsteen in further view of Kensil (March 1999). Kensil is alleged to teach QS-21 as an adjuvant. Insofar as claim 133 is alleged to have been obvious over Chain in combination with other references published before Chain, Chain is not prior art for at least the same reasons as discussed in connection with claim 119.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,

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